

Accepted Manuscript

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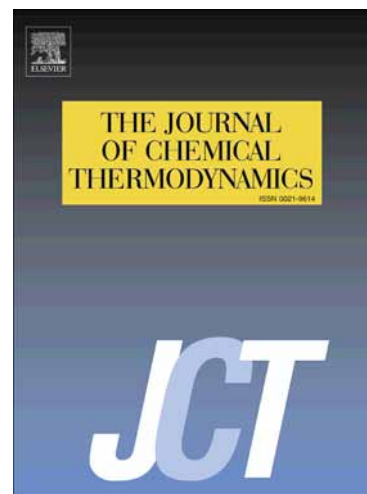
PII: S0021-9614(18)30902-9
DOI: <https://doi.org/10.1016/j.jct.2018.09.008>
Reference: YJCHT 5537

To appear in: *J. Chem. Thermodynamics*

Received Date: 31 August 2018
Accepted Date: 13 September 2018

Please cite this article as: X. Feng, A. Farajtabar, H. Lin, G. Chen, Y. He, X. Li, H. Zhao, Equilibrium solubility, solvent effect and preferential solvation of chlorhexidine in aqueous co-solvent solutions of (methanol, ethanol, N,N-dimethylformamide and 1,4-dioxane), *J. Chem. Thermodynamics* (2018), doi: <https://doi.org/10.1016/j.jct.2018.09.008>

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Equilibrium solubility, solvent effect and preferential solvation of chlorhexidine in aqueous co-solvent solutions of (methanol, ethanol, *N,N*-dimethylformamide and 1,4-dioxane)

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Abstract

The equilibrium solubilities of chlorhexidine in four solvent mixtures of methanol (1) + water (2), ethanol (1) + water (2), DMF (1) + water (2) and 1,4-dioxane (1) + water (2) at temperature range from (278.15 to 318.15) K were reported. At the same composition of methanol, ethanol, DMF or 1,4-dioxane and temperature, the mole fraction solubility of chlorhexidine was highest in DMF (1) + water (2) mixtures, and lowest in ethanol (1) + water (2) mixtures. By using the Jouyban-Acree model, van't Hoff-Jouyban-Acree model and Apelblat-Jouyban-Acree model, chlorhexidine solubility was well correlated obtaining *RAD* lower than 1.69 % and *RMSD* lower than 0.87×10^{-4} . The dissolution process of chlorhexidine in solvent solutions was endothermic for the dissolution process. To study the solvent effect, solubility data were correlated to KAT parameters and cavity term on the basis of linear solvation energy relationships concept. Results indicate the key effect of cavity term and π^* in aqueous methanol and ethanol mixtures; cavity term in aqueous DMF mixtures; and cavity term, β and π^* in aqueous 1,4-dioxan mixtures. Quantitative values for the local mole fraction of methanol (ethanol, DMF or 1,4-dioxane) and water around the

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